

We claim:

1. An array comprising at distinct locations on a substrate, nucleic acid molecules each selectively binding to a gene comprising a regulatory sequence and a promoter, wherein each promoter interacts with a second nucleic acid molecule binding to the regulatory sequence or whose expression is dependent on this binding.
2. The array of claim 1 wherein the gene comprises sequences encoding proteins associated with a particular state, disease or disorder.
3. The array of claim 2 wherein the state is age.
4. The array of claim 3 wherein the genes are isolated from a young animal.
5. The array of claim 3 wherein the genes are isolated from an old animal.
6. The array of claim 2 further comprising nucleic acid molecules selectively binding to housekeeping genes whose expression does not change significantly as the state changes or with the occurrence of the disease or disorder.
7. The array of claim 6 comprising at least nine housekeeping genes.
8. The array of claim 6 wherein the state is age and the expression of the housekeeping genes does not change as the animals age.
9. The array of claim 8 wherein the housekeeping genes are selected from the group consisting of tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, hypoxanthine phosphoribosyltransferase I (Lesh-Nyhan syndrome), Major histocompatibility complex, class I, C, Ubiquitin C, Glyceraldehyde-3-phosphate dehydrogenase, Human mRNA fragment encoding cytoplasmic actin, 60S Ribosomal protein L13A, and Aldolase C.
10. The array of claim 1 wherein the genes are present in nanomolar quantities.
11. A set of primers for use in detecting changes in expression of genes comprising a regulatory sequence in its promoter or interacting with a gene binding to the regulatory sequence, having a length between 480 and 700 base pairs length and a melting point between 75 and 85°C, wherein the primers

include non-consensus sequence with protein coding sequence so that there is no detectable hybridization between homologous genes.

12. The set of primers of claim 11 where there is no hybridization between homologous genes.

13. The set of primers of claim 11 wherein the primers do not hybridize to homologous genes having the same degree of homology and with the associated genes.

14. The set of primers of claim 11 comprising a label.

15. The set of primers of claim 14 wherein the label is selected from the group consisting of digoxigenine label, radiolabels and fluorescent labels.

16. A kit for detecting changes in expression of genes which is associated with a particular state, disease or disorder comprising

a) an array comprising at distinct locations on a substrate, nucleic acid molecules each selectively binding to a genes each comprising a regulatory sequence in its promoter or interacting with a gene binding to the regulatory sequence and one or more housekeeping genes;

b) a set of primers for use in detecting changes in expression of the genes in the array; and

c) means for detecting hybridization between the primers and the regulatory sequences.

17. The kit of claim 16 wherein the array of genes is prepared from cells or tissues of an animal characterized by a particular state, disease or disorder.

18. The kit of claim 17 wherein the animal is selected based on age or a disease or disorder associated with cancer, the neuronal system, the musculoskeletal system, or cardiovascular system.

19. The kit of claim 17 further comprising means for quantitating the amount of expression.

20. The kit of claim 18 wherein the animal or cells from which the genes are derived have been treated with one or more compounds or dosage regimes to screen for an effect of the compound or dosage regime on the state, disease or disorder.

21. A method of detecting changes in expression of genes associated with a particular state, disease or disorder comprising

- a) providing an array of genes comprising a regulatory sequence in its promoter or interacting with a gene binding to the regulatory sequence;
- b) providing a set of primers for use in detecting changes in expression of genes comprising a regulatory sequence in its promoter or interacting with a gene binding to the regulatory sequence, having a length between 480 and 700 base pairs length and a melting point between 75 and 85°C, wherein the primers include non-consensus sequence with protein coding sequence so that there is no detectable hybridization between homologous genes comprising a label;
- c) providing the array of genes comprising a regulatory sequence in its promoter or interacting with a gene binding to the regulatory sequence and sequences encoding proteins associated with a particular state, disease or disorder further comprising housekeeping genes whose expression does not change significantly as the state, disease or disorder changes; and
- d) reacting the primers with the genes.

22. A method for screening for differential expression of one or more regulatory genes or genes interacting with genes binding to the regulatory sequence, comprising:

- a) providing a first library associated with a particular disease, disorder or state,
- b) providing a second library of DNA obtained from cells having a different state or exposed to a compound to be tested,
- c) detecting or measuring expression of selected genes in the second library,
- d) comparing the expression of the selected genes in the first and second libraries, and
- e) detecting which genes have altered expression in the second DNA library.

23. The method of claim 22 wherein the state is selected from the group consisting of age, cancer and diseases or disorders of the cardiovascular, neurological, musculoskeletal, systems.
24. The method of claim 22 wherein the compound is a drug or toxin.
25. The method of claim 22 further comprising normalizing results of expression by comparison with housekeeping genes.
26. A method for determining the effect of a compound, disease or state of an individual comprising:
- a) providing a DNA library including one or more regulatory genes or genes interacting with genes binding to the regulatory sequence from the individual after treatment of the individual, cells or tissues derived therefrom with the compound or a particular dosage regime of the compound,
  - b) screening the library for changes in levels of expression of the selected genes, and
  - c) correlating the changes in expression with the state, disease or disorder prior to treatment.
27. The method of claim 26 wherein the cells or tissues are treated with one or more compounds *in vitro* prior to making the DNA library.
28. The method of claim 26 wherein the compound is selected from the group consisting of proteins or peptides, sugars or polysaccharides, nucleic acid molecules, and synthetic molecules.
29. The method of claim 26 wherein the library is derived from cells obtained from an individual of a particular age, having a particular disease or disorder, or derived from the neurological system, the cardiovascular system, the musculoskeletal system, or cancerous tissues.
30. A microarray comprising discrete samples of nucleotide molecules hybridizing to the genes of proteins whose expression is under the control of the same regulatory element, selected from the group consisting of genes whose non-coding region contains the same defined nucleotide bases for enhancers or repressors to bind to and genes whose protein products can bind to designated regulatory sequences.

31. The microarray of claim 30 further comprising control genes that are not under the control of the same regulatory element.

32. The microarray of claim 30 wherein the regulatory element is an enhancer or promoter.

33. The microarray of claim 30 wherein the regulatory element is selected from the group of regulatory elements consisting of osmotic response element, retinoic acid response element, conserved proximal sequence element, vitamin D response element, sterol response element, TNF-alpha response element, serum response element, cAMP response element, antioxidant response element, glucocorticoid modulatory element, gonadotropin-releasing hormone-response element, pheromone response element, insulin response element, interferon consensus response element, estrogen response element, hypoxia response element, E2F transcription factor, xenobiotic response element, endoplasmic reticulum stress response element, iron-response element, androgen response element, stress response element, RAS-responsive element binding protein 1, and transforming growth factor, beta-1 response element.

34. A method for screening for genes whose expression is altered by disease, age, or exogenous agent comprising screening a sample comprising genes from a library, cells or animal exposed to the disease, age or exogenous agent for binding to a microarray comprising discrete samples of nucleotide molecules hybridizing to the genes of proteins whose expression is under the control of the same regulatory element.

35. The method of claim 34 wherein the microarray further comprises control genes that are not under the control of the same regulatory element.

36. The method of claim 34 wherein the regulatory element is selected from the group of regulatory elements consisting of osmotic response element, retinoic acid response element, conserved proximal sequence element, vitamin D response element, sterol response element, TNF-alpha response element, serum response element, cAMP response element, antioxidant response element, glucocorticoid modulatory element, gonadotropin-releasing hormone-response element, pheromone response element, insulin response element, interferon

consensus response element, estrogen response element, hypoxia response element, E2F transcription factor, xenobiotic response element, endoplasmic reticulum stress response element, iron-response element, androgen response element, stress response element, RAS-responsive element binding protein 1, and transforming growth factor, beta-1 response element.

37. The method of claim 34 further comprising comparing the levels of expression of the genes from a library, cells or animal exposed to the disease, age or exogenous agent, with the levels of expression of the genes from a library, cells or animal not exposed to the disease or exogenous agent, or of a different age.

38. The method of claim 34 wherein the disease is selected from the group consisting of neurological disorders, cardiovascular disorders, bone and muscle disorders, blood or circulation related disorders, and cancer.

39. The method of claim 38 wherein the diseases are selected from the group consisting of Alzheimer's disease, Parkinson's disease, Huntington's disease, myocardial hypertrophy, atherosclerosis, myocardial infarction, osteoarthritis, osteoporosis, and autoimmune disorders.

40. The method of claim 38 wherein the cancers are selected from the group consisting of breast cancer, prostatic hypertrophy, prostatic cancer, colon cancer, chronic lymphocytic leukemia, acute lymphocytic leukemia, brain tumors, pancreatic cancer, and hepatomas.

41. A method of making a microarray comprising primers hybridizing to a target nucleic acid molecule, the method comprising

attaching primers to discrete sites on the microarray,

wherein the primers include at least eight to fifteen bases of sequence found within approximately 1000 bases from a target feature of between 400 and 5000 bases, having a core similarity of greater than 0.95 and a matrix similarity of greater than 0.85, and having significant alignment to the target nucleic acid molecule but not to other genes or clones.